Appl. No. 10/792,176 Amdt. dated September 14, 2007 Reply to Office Action of April 30, 2007

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

Claims 1-63. (Canceled)

64. (Currently amended) A method for identifying a covalent modification of an amino acid residue in a polypeptide ehain comprising:

detecting a mass-difference between a formed polypeptide and a modified polypeptide by mass spectrometry, wherein the modified polypeptide comprises a covalent modification of an amino acid residue in the formed polypeptide, whereby the mass difference identifies the covalent modification.

(1) reacting the polypeptide having a covalent modification with a molar excess of a pair of reagents comprising phenylisothiocyanate (PITC) as a coupling reagent and phenylisothiocyanate (PIC) as a terminating reagent each of which forms a reaction product with a terminal amino acid residue of the polypeptide to be analyzed under a basic reaction condition; the reaction product generated between the terminating reagent and the terminal amino acid residue of the polypeptide being stable under all subsequent reaction conditions;

(2) changing the reaction conditions to acidic conditions so that the PITC terminal amino acid separates from the remainder of the peptide, forming a reaction mixture comprising:

i. unreacted coupling and terminating reagents,

ii. a first reaction product which is the reaction product between the polypeptide and the PIC terminating reagent; and

Appl. No. 10/792,176 Amdt. dated September 14, 2007 Reply to Office Action of April 30, 2007

- <u>iii. a newly formed polypeptide from which the terminal amino acid residue has</u> been removed;
- (3) repeating steps (1) and (2) any selected number of cycles thereby to form a final mixture which comprises:
- i. reaction product between the polypeptide and the PITC terminating reagent, and
- ii. a peptide ladder which is a series of adjacent reaction products which is formed by reaction between the terminating reagent and the terminal amino acid residue of a fraction of the newly generated polypeptide of each cycle; and,
- (4) identifying the covalent modification by determining the differences in molecular mass between adjacent members of the series of reaction products by mass spectroscopy, said differences being equal to the molecular mass of the amino acid residue cleaved from the polypeptide and from each subsequent formed polypeptide of the series, said differences coupled with the positions of said adjacent members in the mass spectrum being indicative of the identity and position of the covalent modification in the polypeptide.
- (Previously presented) The method of claim 64 wherein the covalent modification is phosphorylation.
- (Previously presented) The method of claim 64 wherein the covalent modification is acetylation.
- (Previously presented) The method of claim 64 wherein the covalent modification is glycosylation.
- (Previously presented) The method of claim 64 wherein the covalent modification is a disulfide bond.

Appl. No. 10/792,176 Amdt. dated September 14, 2007 Reply to Office Action of April 30, 2007

- (Previously presented) The method of claim 64, wherein said mass spectrometry is ion trap mass spectrometry.
- 70. (Previously presented) The method of claim 64, wherein said mass spectrometry is quadrupole mass spectrometry.

Claims 71-74 (Canceled).